THE WALTER AND ELIZA HALL INSTITUTE OF MEDICAL RESEARCH

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DIRECTOR: PROFESSOR G. J. V. NOSSAL, F.A.A.

June 7, 1968

Dr. Joshua Lederberg,
Department of Genetics,
Stanford University School of Medicine,
Stanford Medical Center,
PALO ALTO, California, 94304. U.S.A.

Dear Joshua,

I deeply appreciate your courtesy and generosity in allowing Vance Gledhill to join your course and can assure you that, unless my judgement of people is very much astray, he will be a very worthy and articulate participant. Your other suggestion for visits sound good, and I will now take immediate steps to attempt to raise the $2,000 or so that will be necessary for a somewhat more extended trip, and may take you up on the offer of still further visits once the money comes through.

NOSSAL

You may be interested in passing, to hear of some of the work that has been engaging me over the past few months. I am working out a technology for performing protein immunochemistry on single mammalian cells. The technique involves microdrop iodinations using carrier-free $I^{125}$ and subsequent micro-electrophoresis and immuno-electrophoresis followed by autoradiography. It is surprising how much heat one can get in, and we have already got persuasive though not yet publishable evidence that single normal antibody-forming cells do indeed resemble malignant myeloma cells as I guess everyone would have predicted. Microdensitometric scans give impressive profiles with surprising amounts of structure also in the alpha region as well as the expected sharp gamma spike. I believe from the long range point of view a far more important problem will be the application of this technology to problems of differentiation - when does a protein containing embryo cells begin to show inter-cellular heterogeneity? at the 2 cell, 4 cell, 8 cell or 16 cell stage or when? Paul Gross has done something of this general nature using semi micro techniques and some hundreds of cells but the present approach is strictly a single cell one. The main problem that I have struck relates to protein denaturation, which manifests itself both as an acceleration of electrophoretic mobility and a tendency towards aggregation, even though tests are run in 8 M urea. I omitted to mention that iodinations are done by the chloramine-T of Hunter and Greenwood. I know this kind of work is fairly close to your own interests and if you have any passing thoughts on how the methodology could be improved, I

would love to hear from you. The student who is doing this work with me is moving on to Boris Rotman's laboratory next year and I myself will be spending a sabbatical leave at the Pasteur Institute with Alain Bussard who I think you will remember.

Best personal regards,

As ever,

Jim Crow